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Pancreatic VIPomas from China: Case reports and literature review

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ABSTRACT

Vasoactive intestinal polypeptide-secreting tumors (VIPomas) are rare neuroendocrine tumors that often present as watery diarrhea, hypokalemia, and achlorhydria or hypochlorhydria. In this study, we present our institutional experience of diagnosis and treatment of VIPomas, along with a review of the Chinese literature since 1980. Patient #1, diagnosed in 1984 and with intact clinical records, shows the natural history of this disease. Patient #2, diagnosed in 2015, shows the results of evaluation by nuclear medicine techniques and the outcomes of standardized treatment. Comprehensive review of 41 cases allows evaluation of clinical characteristics, treatments and outcomes of pancreatic VIPoma patients. All patients presented with watery diarrhea. The average stool volume reached 3247 mL per day. Average serum VIP level was 839.3 ng/L. Twelve of the 41 cases were reported to have metastases at diagnosis. Somatostatin receptor scintigraphy and ^{18}FDG PET-CT are efficient methods for detection of VIPoma. Surgical excision can promptly alleviate hormonal symptoms.

Introduction

Vasoactive intestinal polypeptide-secreting tumors (VIPomas) are rare functioning neuroendocrine tumors associated with secretory diarrhea. The estimated incidence of VIPoma is about one in ten million people per year [1]. 90% of these tumors in adults arise from the pancreas, although they have also been reported to be in the colon, bronchus, adrenals and sympathetic ganglia [2]. Approximately 70% of the patients are reported to have metastasis at the time of diagnosis, leading to a poor prognosis [3].

VIPoma syndrome is characterized by watery diarrhea, hypokalemia, and achlorhydria or hypochlorhydria, also known as WDHA syndrome. VIPoma syndrome is caused by excessive secretion of vasoactive intestinal peptide (VIP) by the tumor. VIP is a 28-amino acid polypeptide that normally functions as a neurotransmitter [4]. VIP binds to receptors on intestinal epithelial cells, leading to activation of cellular adenylate cyclase through the G protein-coupled pathway. Production of cyclic adenosine monophosphate (cAMP) causes massive secretion of fluid and electrolytes, especially potassium, into the intestinal lumen, resulting in secretory diarrhea, dehydration, hypokalemia and significant weight loss.

Nearly 60 years have passed since the first description of VIPoma. However, due to the low incidence of this tumor, case reports have been our main source of information and knowledge about the disease. In this study, we present two cases of VIPoma in detail. Patient #1 shows the natural history of VIPoma, and patient #2 shows the results of evaluation by nuclear medicine techniques and the outcomes of standardized treatment. We also reviewed the Chinese literature, which helps us analyze the clinical characteristics, treatments and outcomes of pancreatic VIPomas.

Case reports

Patient #1 (diagnosed in 1984): A 27-year-old male presented to our hospital with a 2-month history of watery diarrhea and 10 kg weight loss. He also experienced extreme thirst, with a water intake over 15000 mL and urine volume over 10000 mL per day. Paroxysmal flushing of the face occurred with intermittent headache. Subsequent evaluation revealed a potassium level of 1.7 mmol/L. Gastric fluid analysis showed achlorhydria. Blood glucose was slightly elevated and a urine para-aminobenzoic acid (PABA) test

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Table 1
Gastrointestinal hormone levels of patient#1.

	Value	High-Normal
VIP	231.9–874.1	60 (pg/mL)
Somatostatin	587.5–2338.2	25 (pg/mL)
5-Hydroxytryptamine	198.0–341.0	120 (ng/mL)
Prostaglandin-E	2.88	0.7 (ng/mL)
Pancreatic Polypeptide	19.6–73.8	151 (pg/mL)
Gastrin	77.0–99.9	100 (pg/mL)
Insulin	6–14	25 (μU/mL)

(47.6%, normal value > 60%) showed a decrease of pancreatic exocrine function. Thyroid function tests, parathyroid hormone, growth hormone, and serum cortisol were normal. His serum VIP level reached 874.1 pg/mL, with a serum somatostatin level of 2338.2 pg/mL. Other gastrointestinal hormone levels are presented in Table 1. An abdominal CT scan revealed a mass in the body of his pancreas and multiple hepatic nodules, consistent with hepatic metastasis. After being admitted to hospital, he was treated with large amounts of potassium supplement, which relieved his extreme thirst and his urine volume dropped to 2000 mL per day. Prednisone (40 mg/d) was used to control symptoms but lost effectiveness in several days. Enlargement of his left supraclavicular lymph nodes was discovered two months later and biopsy showed metastasis of the VIPoma. Later, he underwent abdominal laparotomy which showed extensive metastasis of the tumor, preventing resection. Soon, ascites appeared and the abdominal pain was aggravated, and he died because of respiratory and circulatory failure. Autopsy showed extensive metastasis of the neuroendocrine tumor to the liver, lung, cardiac muscle, left adrenal gland, bladder and retroperitoneal tissue, and to the mesenteric and para-aortic lymph nodes.

Patient #2 (diagnosed in 2015): A 60-year-old male presented to an outside hospital with a 2-year history of watery diarrhea and 30 kg weight loss. The patient declared around 6–8 loose bowel movements and an estimated stool volume of 4–6 L per day. His diarrhea was free of fat or blood, and was not stopped by fasting or anti-diarrheal drugs. Two months ago, the patient developed aggravated disease symptoms. His stool volume increased to 11–12 L per day, and this was associated with facial flushing and muscle weakness. Laboratory findings revealed severe hypokalemia, with a potassium level of 1.51 mmol/L. A contrast-enhanced CT scan (Fig. 1) showed a 5.7 × 3.7 cm mass at the head of the pancreas with a clear border and heterogeneous enhancement. The mass compressed the main pancreatic duct and common bile duct, causing distal pancreatic atrophy and gallbladder enlargement. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) (Fig. 1) also identified an equal T1 and long or equal T2 signal at the head of the pancreas, with clear borders and homogenous enhancement. No sites of distant metastases were identified. He underwent ^{68}Ga-DOTATATE PET-CT, which showed high expression of somatostatin receptor at the pancreatic mass, indicating a possible neuroendocrine tumor (Fig. 2). Before surgery, he was treated with Octreotide 0.2 mg every 8 h, and his diarrhea improved substantially. The patient underwent pancreatoduodenectomy. Octreotide was reduced to 0.1 mg iv q8h after surgery, and was stopped seven days later. Diarrhea did not reoccur and serum K+ rose to 3.6 mmol/L. Histological examination revealed a G2 neuroendocrine tumor (NET) (Ki-67 index 7%) with

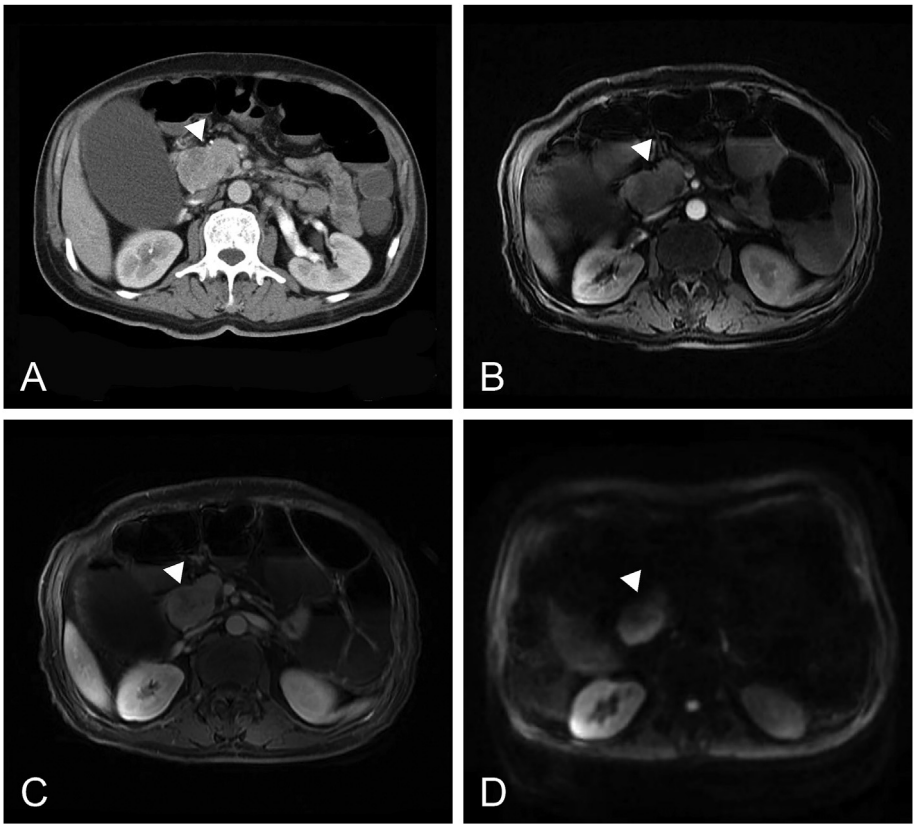

Fig. 1. Preoperative imaging. A, Contrast-enhanced CT scan showing a 5.7 × 3.7 cm mass (triangle) at the head of the pancreas with clear border and heterogeneous enhancement, compressing the main pancreatic duct and common bile duct. B, DCE-MRI identifying a mass at the head of the pancreas in arterial phase. C, Portal phase. D. Diffusion-weighted MRI (DWI).

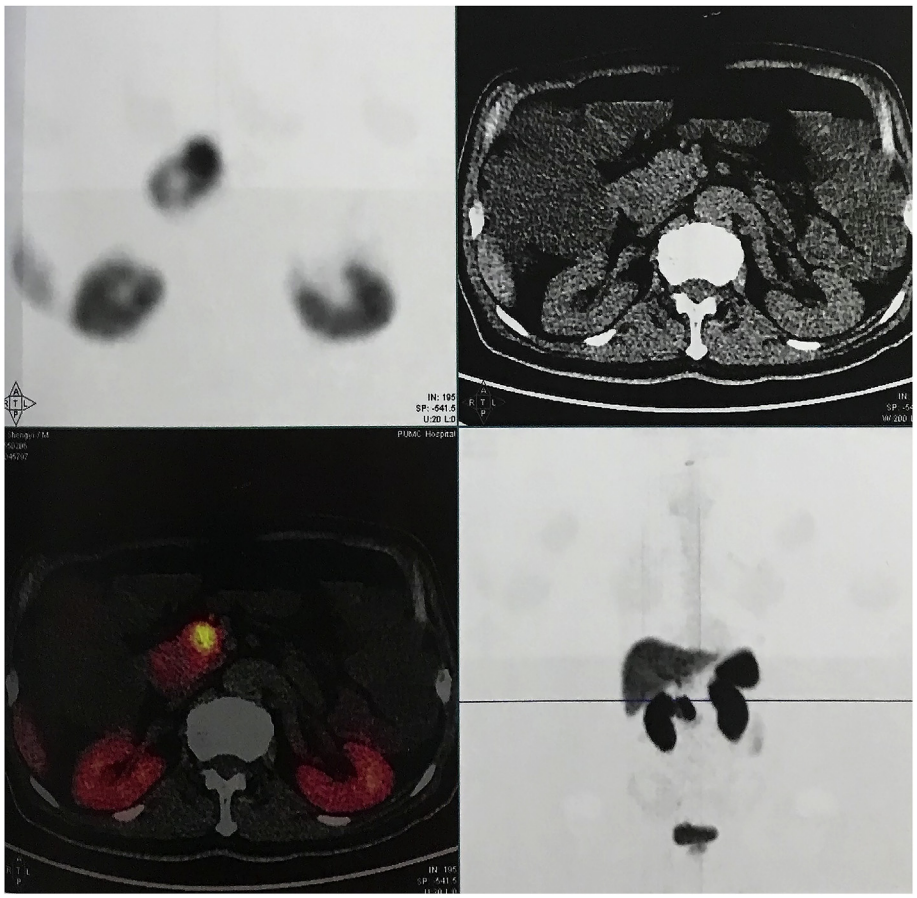

Fig. 2. ^{68}Ga-DOTATATE PET-CT showing high expression of somatostatin receptor at the pancreatic mass.

no metastases to the regional lymph nodes. Immunohistochemistry staining showed VIP(+++), Syn(+), Gastrin(±), Glucagon(−), Insulin(−), Somatostatin(−). He was treated with monthly administration of 20 mg Octreotide LAR, and there was no sign of diarrhea recurrence until now.

Literature review

In our review of the Chinese literature from 1980 to 2017, we found 27 case reports and one case series. With the addition of five cases from Peking Union Medical College Hospital, there are 41 reports in total of patients with pancreatic VIPoma. This is the first paper to summarize and analyze the Chinese VIPoma cases so extensively. Information about the 41 patients is summarized in Table 2 [5–29].

Age and sex: Among the 41 patients, there were 18 females and 23 males, ranging in age from 27 to 82 years (mean 52.4 ± 13.5).

Clinical presentations: 100% of the patients presented with watery diarrhea. The average stool volume reached 3247 ± 1876 mL per day. In the 10 cases that only reported defecation frequency, the average was 12.6 stools per day. 30% of the patients complained about fatigue or muscle weakness, and 20% experienced facial flushing. One patient suffered from polydipsia and polyuria possibly due to hypokalemic nephropathy. Laboratory tests revealed an average serum potassium level of 2.02 ± 0.52 mmol/L, which showed little improvement when treated merely with oral or intravenous repletion. Serum VIP levels were reported in 28 cases, and the average value was 839.3 ± 1104.9 ng/L.

Site and size: Seventeen of the primary tumors were found in the head of the pancreas, and 24 were in the body or tail of the pancreas. The primary tumors ranged in size from 2.3 to 11 cm, and the average size of the primary tumor was 5.7 ± 1.9 cm.

Metastasis: Twelve of the 41 (29.3%) cases were reported to have metastases at the time of diagnosis, of which 100% were located in the liver. Two cases had metastases in the regional lymph nodes, and one case (Patient #1) experienced extensive metastasis as defined earlier. The presence of metastases portends a significantly worse prognosis. Three patients that were reported dead all presented with unresectable metastases that grew large and caused lethal hormonal symptoms.

Diagnosis: The average time from symptom presentation to final diagnosis was about 15 months. Most tumors were positive in CT scans or MRI. One patient from our hospital underwent somatostatin receptor scintigraphy (SRS) with an indicative result for NET, and three patients that underwent ^{18}FDG PET-CT all showed increased uptake of ^{18}FDG.

Histology: Histology reports were not complete in most of the case reports. Only the two most recent cases from our hospital reported the Ki-67 index and the number of mitoses. Both cases were graded as G2 NET; however, one patient experienced liver metastasis and ended up with a poor prognosis, while the other patient did not show evidence of recurrence after excision of the primary tumor.

Treatment: Surgical resection of the primary tumor was performed in 36 of 41 cases (87.8%). The procedures included distal pancreatectomy (13, 31.7%), pancreaticoduodenectomy (7, 17.1%),

Table 2
Cases from our hospital and previously published case reports/case series of pancreatic VIPomas in the Chinese literature.

Ref.	Year of publication	Age, y/Sex	Stool volume (mL/d)	Stool frequency (/day)	Serum K+ (mmol/L)	Imaging	Size (cm)	Site of pancreas	Metastases	Surgery	Serum VIP (pg/ml)	Somatostatin analog treatment
Chen et al.#1	–	60/M	8000	–	1.51	CT,MRI,SRS	4	Head	None	PDD	–	Octreotide
Chen et al.#2	–	58/M	800	–	1.3	MRI,^{18}FDG PET-CT	5	Tail	Liver	DP, LR	–	Octreotide
Chen et al.#3	–	27/M	2400	–	1.7	–	6	Body	Liver	Biopsy	874	None
Chen et al.#4	–	64/M	–	–	1.3	–	–	–	Liver	DP	–	None
Chen et al.#5	–	59/M	2000	–	–	–	–	Head	Liver	PDD	–	None
Niu et al. [7]	2017	34/M	3000	–	2.7	CT	6	Body	–	Electroporation	498	Octreotide
Zhang et al. [8]	2016	65/M	–	10	2.26	CT,^{18}FDG PET-CT	5	Head	Liver	PDD	600	Octreotide
Li et al. [9]	2015	(1) 58/F	–	(1) 20	(1) 1.55	(1) CT	(1) 8	(1) Tail	None	(1) DP	(1) 632	Octreotide
		(2) 82/M		(2) 12	(2) 2.18	(2) CT	(1) 7	(1) Tail		(2) DP	(2) 483	
Li et al. [10]	2014	(1) 73/M	–	(1) 10	(1) 1.9	(1) CT	(1) 5	(1) Head	(1) Liver	(1) PDD, LR	(1) 6214	Octreotide
		(2) 63/M		(2) 10	(2) 2.97	(2) CT,^{18}FDG PET -CT	(2) 5	(2) Head	(2) Liver	(2) Biopsy	(2) 600	
Yue et al. [11]	2014	62/F	–	–	–	–	4	Tail	None	DP	–	Octreotide
Zhou et al. [12]	2013	48/F	1000	–	2.28	CT	5	Tail	None	DP	342	Octreotide
Zhang et al. [13]	2013	48/F	–	10	2.23	CT,EUS	5	Tail	None	DP	260	Octreotide
Guan et al. [14]	2012	69/F	2000	–	2.8	CT,MRI	11	Head	None	PDD	989	Octreotide
Feng et al. [15]	2012	58/M	–	10	1.82	MRI	9	Tail	None	DP	–	Octreotide
Wang et al. [16]	2010	70/M	4000	–	1.9	CT	5	Head	None	Enuc	–	Octreotide
Song et al. [17]	2008	(1) 43/F	(1) 3000	–	(1) 1.1	CT	(1) 6	(1) Head	(1) None	(1) PDD	(1) –	(1) None
		(2) 59/F	(2) 1000		(2) 2.5		(2) 2.5	(2) Body & Tail	(2) None	(2) DP	(2) 390	(2) Octreotide
		(3) 69/M	(3) 1500		(3) 1.9		(3) 5	(3) Head	(3) Liver	(3) Enuc, LR	(3) 1490	(3) Octreotide
		(4) 51/F	(4) 5000		(4) 1.8		(4) 5	(4) Body	(4) Liver	(4) Biopsy	(4) -	(4) None
Luo et al. [18]	2008	53/M	–	–	2.8	–	5	Head	None	Enuc	821	None
Li et al. [19]	2007	28/F	2000	–	1.6	CT, MRI	7	Body	None	DP	–	Octreotide
Jiang et al. [20]	2005	61/M	–	4	2.1	CT	5	Head	None	None	–	None
Li et al. [21]	2004	56/M	6000	–	–	–	5	Head	Liver, LN	PDD, LR	–	None
Ling et al. [22]	2004	59/M	–	20	2.3	–	5	Tail	Liver	DP	680	Octreotide
Zhao et al. [23]	2003	39/F	2500	–	2.28	CT	7	Tail	None	Enuc	–	None
Fang et al. [24]	2003	55/M	3000	–	3.17	CT	6	Tail	None	DP	690	Octreotide
Bai et al. [25]	1999	33/F	–	20	1.3	CT	9	Tail	None	DP	304	None
Liu et al. [26]	1998	58/F	3000	–	2.08	CT	8.5	Tail	None	Enuc	765	None
Zhao et al. [27]	1997	54/M	3000	–	1.8	CT,MRI	6	Head	Liver	Enuc	944	Octreotide
Li et al. [28]	1996	66/F	6000	–	1.63	CT	4.5	Tail	None	Enuc	895	None
Lu et al. [29]	1989	39/F	5000	–	1.63	CT	6.5	Tail	None	DP	429.3	None
Hua et al. [30]	1979	29/M	4000	–	2.2	–	10	Tail	None	Enuc	–	None

(*continued on next page*)

Table 2 (*continued*)

Ref.	Year of publication	Age, y/Sex	Stool volume (mL/d)	Stool frequency (/day)	Serum K+ (mmol/L)	Imaging	Size (cm)	Site of pancreas	Metastases	Surgery	Serum VIP (pg/ml)	Somatostatin analog treatment
Ou et al. [31]	2014	(1) 53/F	–	–	–	–	(1) 3.6	(1) Body	–	(1) Enuc	(1) 518	Octreotide in 60% pts
		(2) 35/M					(2) 2.3	(2) Head		(2) Enuc	(2) 371	
		(3) 33/F					(3) 4.5	(3) Tail		(3) DP	(3) 538	
		(4) 38/F					(4) 7.0	(4) Tail		(4) DP	(4) 679	
		(5) 50/M					(5) 3.2	(5) Head		(5) Enuc	(5) 465	
		(6) 47/F					(6) 5.5	(6) Head		(6) Enuc	(6) 612	
		(7) 42/M					(7) 4.8	(7) Head		(7) PDD	(7) 577	

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; EUS, endoscopic ultrasonography; PDD, pancreaticoduodenectomy; DP, distal pancreatectomy; LR, liver resection; Enuc, enucleation.

and tumor enucleation (16, 39.0%). Liver resection for metastatic tumors was performed in four cases. 24 cases received administration of somatostatin analogs before surgery, and the hormonal symptoms were successfully controlled in all of them. The commonly used dosage was 0.1–0.2 mg of Octreotide three times per day. In most of the cases, diarrhea ceased within three days.

Discussion

VIPomas are rare neuroendocrine tumors that present with characteristic symptoms. In this study, we summarized 41 VIPoma cases from China. Compared with the case reports from the western population [30], few differences were found in the demographics of patients or the site and size of the tumor. However, in an American study published in 2008, the metastatic rate was 19/32 (59%) [30], slightly higher than the rate in our study (29.3%). This may possibly be attributed to the development and popularization of diagnostic techniques in recent years. However, our study also showed that pathological grading and treatment of VIPoma in China are not as standardized as in western countries, reflecting the lack of knowledge of this disease.

Although VIPoma patients share a range of distinctive symptoms, early diagnosis still seems difficult. Our study showed that the average time from symptom presentation to final diagnosis was more than 15 months. Most patients already have large tumors at the time of diagnosis, and the tumors are metastatic in nearly 30% of cases. The truth is that it takes time to develop hormonal symptoms. The half-life of VIP in the circulation is less than one minute and the plasma level of VIP in normal individuals is quite low. Thus, at the time when hormonal symptoms appear, the tumor burden is often large. Due to the rarity of cases, it is not practicable to set up screening projects for neuroendocrine tumors. Therefore, increasing the awareness of physicians and popularizing gastrointestinal hormone measurement is very important to avoid delayed diagnosis.

Nuclear medicine techniques, mainly including somatostatin receptor scintigraphy and PET-CT, are generally recommended for detection and staging of NETs [31]. However, this technique is not widely available in China yet. Among the 41 cases in our study, only four patients underwent nuclear medicine imaging. One patient from our institution received SRS using ^{99}mTc-HTOC as the tracer, and another patient underwent ^{68}Ga-DOTATATE PET-CT. Both patients (G2) showed a positive result, indicating an acceptable sensitivity for nuclear medicine techniques in the diagnosis of VIPomas.

Surgery is the treatment of choice for VIPomas and standardized pancreatic resection is recommended. According to ENETS guidelines, parenchyma-sparing resection is indicated only for insulinomas and small pancreatic NETs with tumor size <2 cm [32]; however, 16 patients (39%) from our study received tumor enucleation. In terms of biological behavior, VIPomas are more malignant than the other more common functional pancreatic NET, insulinoma. Standardized surgical performance should therefore be emphasized. Due to the high metastasis rate of VIPoma, radical surgery is often difficult. In our study, liver metastasis presented in 30% of the cases, while only four of the 12 cases with liver metastasis received liver resection. However, in VIPoma patients, a huge tumor burden often leads to extensive hormonal effects that can possibly cause multiple organ failure. Thus, we believe that cytoreductive surgery is effective for prompt alleviation of symptoms, though long-term outcomes are unknown.

Somatostatin analogs (SSAs) (e.g. Octreotide, Lanreotide) inhibit the secretion of VIP, and thus are considered the drug of choice to control hormonal symptoms for NETs, especially in VIPoma [33]. It has been reported that 80–90% of VIPoma patients improve promptly after administration of somatostatin analogs, which is similar to our study [34]. However, due to the rarity of VIPoma, it has been impossible to establish a sizable cohort to verify the association of symptom control and survival time. Nevertheless, numerous studies on other functional NETs have demonstrated that controlling the excessive hormone state is crucial to lower both morbidity and mortality [35,36]. Also, our case report showed that without controlling the excessive hormone state in VIPoma, the patient could rapidly progress to lethal electrolyte disturbance and organ failure. Thus, using the short-acting somatostatin analog Octreotide as soon as possible should be a reasonable treatment strategy.

To conclude, VIPomas are rare tumors with characteristic symptoms; however, they often progress to unresectable metastatic conditions. Therefore, it is important to consider functional NETs during evaluation of watery diarrhea. Nuclear medicine techniques are effective additional tools for detection and staging of the tumor. Standardized surgery in the only curative treatment, while cytoreductive surgery may provide several benefits. Somatostatin analogs are recommended to control symptoms before surgery. A review of the Chinese language literature showed a lack of standardized pathological grading and treatment of VIPoma, reflecting the lack of knowledge about NETs. Therefore, it is still necessary to raise awareness of related diseases among doctors.

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References

[1] Friesen SR. Update on the diagnosis and treatment of rare neuroendocrine tumors. Surg Clin 1987;67:379–93.
[2] Ectors N. Pancreatic endocrine tumors: diagnostic pitfalls. Hepato-Gastroenterology 1999;46:679–90.
[3] Mekhjian HS, O'Dorisio TM. VIPoma syndrome. Semin Oncol 1987;14:282–91.
[4] Umetsu Y, Tenno T, Goda N, Shirakawa M, Ikegami T, Hiroaki H. Structural difference of vasoactive intestinal peptide in two distinct membrane-mimicking environments. Biochim Biophys Acta 2011;1814:724–30.
[5] Niu L, Li J, Zeng J, Fang G, Zhou L, Xu K, et al. Percutaneous irreversible electroporation for pancreatic VIPoma: a case report. Pancreas 2017;46:135–7.
[6] Zhang X, Zhou L, Liu Y, Li W, Gao H, Wang Y, et al. Surgical resection of vasoactive intestinal peptideoma with hepatic metastasis aids symptom palliation: a case report. Exp Ther Med 2016;11:783–7.
[7] Li JB, Xie RJ, Liu SB. Two cases of pancreatic VIPoma. Chin J Gen Surg 2015;30.
[8] Li YJ, Wang KW, Zhou JP, Kong FM, Tian YL, Dong Y. Diagnosis and treatment of pancreatic vasoactive intestinal peptide tumor (report of 3 cases). Chin J Bases Clin Gen Surg 2014;21:633–5.
[9] Yue PJ, Su AP, Zhang Y, Yang M, Wang L, Tian BL. Vasoactive intestinal peptide secreting tumors: report of one case and retrospective analysis of data in literature. Chin J Bases Clin Gen Surg 2014;21:488–91.
[10] Geng Z. One case report of VIPoma. Health 2013;7:282.
[11] Zhang LP, Wu HC, Luo L. Pancreatic vasoactive intestinal polypeptide-secreting tumor: a case report. World Chin J Dig 2013;21:2117–20.
[12] Xiang G, Liu X, Tan C, Zhang H, Mai G, Zheng Z. Diagnosis and treatment of VIPoma: a case report and literature review in China. Pancreas 2012;41:806–7.
[13] Feng XL, Peng JY, Hu Y, Liu AX, Tian L, Zhang H. One case report of VIPoma. Chin Arch Gen Surg (Electronic Edition) 2012;6:425–6.
[14] Wang ZS, Wu LQ, He JS, Guo WD, Zhang S, Cao JY, et al. Pancreatic VIPoma, one case report and literature review. Chin J Gen Surg 2010;19:330–2.
[15] Song SW, Shi R, Zhao N, Liu YF. Vasoactive intestinal peptide-secreting-tumor, report of 4 cases. Chin J Gen Surg 2008;23:340–2.
[16] Luo GP, Jin C, Fu LD, Di Y, Long J, Ni QX. One case report of VIPoma. Chinese Journal of Practical Surgery 2008;28:237–8.
[17] Li M, Xie BY, Zhou LQ, Shi W, Zhang ZT. VIPoma, one case report and review of literature. Chin J Dig 2007;27:125–6.
[18] Jiang TC, Mao XM. One case report of malignant pancreatic VIPoma. Radiol Practice 2005;20:1111–2.
[19] Li JT, Peng SY, Liu YB, Fang HQ, Wu YL, Wang XB, et al. Diagnosis and treatment of vasoactive intestinal peptide-secreting tumors: one case report and 15 years review in China. Chin J Surg 2004;42:524–7.
[20] Xiaohua L. One case report of VIPoma. Chinese Journal of Digestion 2004;24:634.
[21] Zhao XS, Zhou M, Dou B. One case report of pancreatic VIPoma. Journal of Clinical Radiology 2003;22:243.
[22] Fang WL, Wu YL. One case report of VIPoma. Chinese Journal of Practical Internal Medicine 2003;23:625.
[23] Bai HW, Ma YL, Gui RY. One case report of VIPoma. Chin J Surg 1999;37:134.
[24] Liu CY, Han JP, Shen WH. One case report of VIPoma. Chinese Journal of Digestion 1998;18:203.
[25] Zhao YP, Wu B, Cai LX, Zhong SX, Zhu Y. Pancreatic vasoactive intestinal peptide tumor syndrome. Pu Wai Lin Chuang 1997;12:15–9.
[26] Li J, Wang C. One case report of VIPoma. Chin J Gastroenterol Hepatol 1996;5:308+305.
[27] Lu WK, Mao TS. One case report of VIPoma. Chin J Endocrinol Metab 1989;5:53–4.
[28] Hua EQ, Jiang YJ. WDHA syndrome, a case report. Xin Yi Xue 1979;11:95–6.
[29] Ou DP, Yang LY, Hua D, Xia Z, Wu DF. Diagnosis and surgical treatment for pancreatic vasoactive intestine polypeptide tumor. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2014;39:1045–8.
[30] Ghaferi AA, Chojnacki KA, Long WD, Cameron JL, Yeo CJ. Pancreatic VIPomas: subject review and one institutional experience. J Gastrointest Surg 2008;12:382–93.
[31] Sundin A, Arnold R, Baudin E, Cwikla JB, Eriksson B, Fanti S, et al. ENETS consensus guidelines for the standards of care in neuroendocrine tumors: radiological, nuclear medicine & hybrid imaging. Neuroendocrinology 2017;105:212–44.
[32] Partelli S, Bartsch DK, Capdevila J, Chen J, Knigge U, Niederle B, et al. ENETS consensus guidelines for standard of care in neuroendocrine tumours: surgery for small intestinal and pancreatic neuroendocrine tumours. Neuroendocrinology 2017;105:255–65.
[33] O'Dorisio TM, Anthony LB. A 25-year experience of gastroenteropancreatic neuroendocrine tumors and somatostatin (congeners) analogs: from symptom control to antineoplastic therapy. Front Horm Res 2015;44:177–92.
[34] O'Toole D, Salazar R, Falconi M, Kaltsas G, Couvelard A, de Herder WW, et al. Rare functioning pancreatic endocrine tumors. Neuroendocrinology 2006;84:189–95.
[35] Ito T, Igarashi H, Uehara H, Jensen RT. Pharmacotherapy of zollinger-ellison syndrome. Expet Opin Pharmacother 2013;14:307–21.
[36] Jensen RT, Niederle B, Mitry E, Ramage JK, Steinmüller T, Lewington V, et al. Gastrinoma (duodenal and pancreatic). Neuroendocrinology 2006;84:173–82.